UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/646,924	09/25/2000	Eric Raspe	MERCK 2157	2859

23599 7590 07/01/2002

MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	PAPER NUMBER
1637	13

DATE MAILED: 07/01/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/646,924	Applicant(s) RASPE ET AL.	
	Examiner Suryaprabha Chunduru	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicants' response to the office action and amendment (Paper No. 12) filed on April 11, 2002 has been entered.

Response to Arguments

2. Applicant's response to the office action (Paper No.12) is fully considered and deemed persuasive in part.

3. The rejection made under 35 U.S.C. 112 second paragraph in the previous office action is withdrawn herein in view of the applicants' amendment (Paper No.12).

4. The rejection made in the previous office action under 35 U.S.C. 112, first paragraph written description, is maintained herein because of the following reasons:

The instant claims 1-22 are drawn to a method of screening a substance comprising regulation of apo C-III gene via ROR receptor or a response element of ROR receptor thereof. Applicants' argue that of the removal of the phrase 'functional equivalents thereof" would obviate the rejection, which is found not persuasive because ROR receptor family itself is a genus, which comprises various binding sites for a number of different substances which inturn could regulate apo C-III gene. As described in the specification (page 1, lines 23-28), ROR receptor exists in three forms and each form binds to a specific response element, and modulate the transcription of their target genes. Further, the specification describes that RORα receptors are involved in the regulation of the expression of the apo C-III gene. Thus applicants have shown one species of ROR receptor that can interact with a substance to regulate the apo C-III gene. No information was given in the specification regarding the involvement of other ROR family receptors, which regulate the expression of apo C-III gene. Thus the claims read broadly

on ROR family receptors and do not meet the written description guidelines and hence the rejection is maintained herein.

5. The rejection made in the previous office action under 35 U.S.C. 112, first paragraph, scope of enablement, is withdrawn herein in view of the amendment (Paper No. 12).

6. With respect to the rejection made in the previous office action under 35 U.S.C. 103(a), Applicant's arguments with respect to claims 1-22 are considered but are moot in view of the new ground(s) of rejection based on the amendment.

New Grounds of Rejection necessitated by Amendment

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Karathanasis et al. (USPN. 5,721,096) and in view of Fraser et al. (J Biol Chem., Vol. 272 (21): 13892-13898, 1997).

Karathanasis et al. teach a method for screening a compound, which alters apolipoprotein AI gene expression, wherein Karathanasis et al. disclose that the method comprises (i) contacting said compound with cells comprising ROR receptor, or a response element involved in regulation of apo AI gene and measuring the level of apo AI gene expression as an indication of said compound having ability to alter said gene expression (see column 31, lines 55-67, column 17, lines 13-26, column 8, lines 17-56). Karathanasis et al. also teach contacting the said compound to a nuclear factor and a response element and measuring the binding complex formed with nuclear factor and assessing the ability of the said compound to alter or modulate the said gene expression (see column 33, lines 3-22, column 21, lines 8-22); transfection with a DNA fragment operably linked to a promoter and a reporter gene under the control of said promoter (see column 14, lines 40-67, column 31, lines 55-67, column 2, lines 14-37, column 3, lines 41-53); competitive binding of ligand to ROR (see column 16, lines 8-33, column 9, lines 1-25); the method of screening compounds could play a role in regulation of cholesterol and lipid metabolism (see column 5, lines 29-37, column 17, lines 62-67, column 8, lines 1-12). Karathanasis et al. also indicates that cis-acting elements of apo AI regulatory protein-1 (binds to ROR receptor) binds with apo CIII with high affinity, suggesting this protein may be involved in the regulation of apo AI, apo CIII, apoB, insulin and ovalbumin genes (see column 12, lines 28-43). However, Karathansis et al. did not teach expression of apo CIII gene in screening a compound useful for altering lipid metabolism.

Fraser et al. teach a method for modulating apo C-III gene expression in the presence of a hepatocyte nuclear factor 4 (HNF-4), a member of ROR family, wherein Fraser discloses that HNF-4 binds to apolipoprotein promoter sequences (based on recombinant promoter-reporter constructs) and induction of apo C-III expression by HNF-4 (see page 13897, paragraph 1 and page 13898, paragraph, 2). Fraser et al. also disclose that the high levels of apo C-III correlate with increased fasting triglycerides in both clinical hypertriglyceridemic patients and murine model systems and the high serum triglycerides are directly atherogenic (see page 13898, paragraph 2). Further, Fraser et al. disclose the modulation of apo C-III expression via HNF-4 might represent a potential therapeutic target (see page 13898, paragraph 2).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of screening compounds that bind to RXR/ROR receptor family as taught by Karathanasis et al. with the method of modulation of apo C-III expression via HNF-4 as taught by Fraser et al. which is applicable to the treatment of atherosclerosis because Karathanasis et al. states that 'apo AI regulatory protein-1 (ARP-1) can interact with cic-acting elements of other genes . ARP-1 bound with high affinity and specificity to COUP (chicken ovalbumin), apo CIII, apo B, insulin, which suggests that the protein may be involved in the regulation of apo AI, apo CIII, apo B, insulin and ovalbumin genes" (see column 12, lines 28-43). One such binding affinity with apo CIII gene, expressly motivated by Fraser et al. is to use human nuclear factor (ROR family member) in regulating apo CIII expression. . An ordinary practitioner would have been motivated to combine the method of Karathanasis et al. with the method of Fraser et al. in order to achieve the expected advantage of a rapid and sensitive method for screening compounds that bind to RXR/ROR.

No claims are allowable.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-0294 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
June 26, 2002

JEFFREY FREDMAN
PRIMARY EXAMINER